

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

MALVERN PANALYTICAL INC.,)	
)	
Plaintiff,)	
)	
v.)	C.A. No. 19-2157 (RGA)
)	
TA INSTRUMENTS-WATERS LLC and)	DEMAND FOR JURY TRIAL
WATERS TECHNOLOGIES CORPORATION,)	
)	
Defendants.)	

FIRST AMENDED COMPLAINT FOR PATENT INFRINGEMENT

Plaintiff Malvern Panalytical, Inc. (“Malvern”) files this Complaint against Defendants TA Instruments-Waters LLC and Waters Technologies Corporation (“Defendants”) and alleges as follows:

NATURE OF THIS ACTION

1. This is a civil action for the infringement of United States Patent Nos. 8,449,175 (the “’175 Patent”), 8,827,549 (the “’549 Patent”), 9,404,876 (the “’876 Patent”), 10,036,715 (the “’715 Patent”), and 10,254,239 (the “’239 Patent”) (collectively, the “Asserted Patents”) pursuant to the patent laws of the United States, 35 U.S.C. § 1 et seq.

PARTIES

2. Plaintiff Malvern is a corporation duly organized and existing under the laws of the Commonwealth of Massachusetts, having its principal place of business at 117 Flanders Road, Westborough, MA 01581. Malvern is the owner by assignment of the Asserted Patents.

3. Malvern is a leading supplier of scientific instruments used for chemical, physical, and structural analysis of materials. Malvern’s technologies are used by scientists and

engineers in a wide range of industries and organizations to solve the challenges associated with maximizing productivity, developing better quality products, and getting products to market faster. On July 22, 2014, Malvern acquired MicroCal LLC (“MicroCal”), a world-leading pioneer in the development and commercialization of microcalorimetry instruments, including isothermal titration calorimeters (“ITCs”). ITCs measure the heat either released or absorbed during chemical reactions, including biomolecular binding events such as when a drug binds to a protein.

4. Upon information and belief, Defendant TA Instruments-Waters LLC (“TA Instruments”) is a corporation organized and existing under the laws of the State of Delaware, with corporate headquarters and a principal place of business at 159 Lukens Drive, New Castle, DE 19720. TA Instruments is a manufacturer of ITC devices. Upon information and belief, Defendant Waters Technology Corporation is a corporation organized and existing under the laws of the State of Delaware, with corporate headquarters and a principal place of business at 34 Maple Street, Milford, MA 01757. Upon information and belief, Waters Technology Corporation is the parent company of TA Instruments. Upon information and belief, Waters Technology Corporation markets and sells infringing ITC devices through its subsidiary TA Instruments.

JURISDICTION AND VENUE

5. This is an action for patent infringement arising under the Patent Act, 35 U.S.C. § 1, et seq., including § 271.

6. This Court has subject matter jurisdiction under 28 U.S.C. § 1331 (federal question), and 28 U.S.C. § 1338(a) (any Act of Congress relating to patents or trademarks).

7. This Court has personal jurisdiction over Defendants, as Delaware is Defendants' state of incorporation.

8. Venue is proper in this District under 28 U.S.C. §§ 1391(b) and 1400(b), as Delaware is Defendants' state of incorporation.

TECHNICAL BACKGROUND

9. Chemical processes, such as the interactions of two compounds, absorb or release energy. This energy may be measured in units of calories. Measuring energy absorbed or released when two compounds interact can reveal important properties about the interaction, such as: (1) binding affinity (the strength of the binding interaction between the two compounds); (2) stoichiometry (the ratio at which any two compounds interact); and (3) binding enthalpy (the amount of energy absorbed or released when two compounds interact). These properties give insight into how a given chemical process works, and are often critical in the development of new chemical products, testing existing products, or simply understanding natural phenomena.

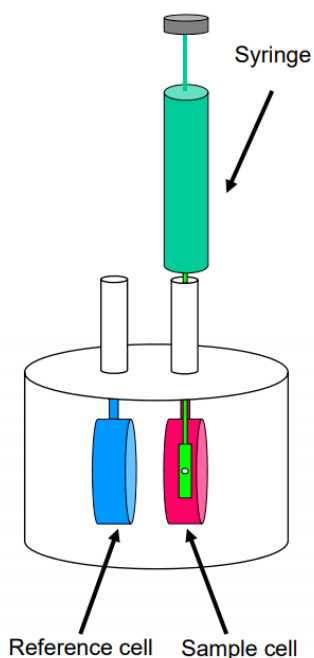
10. Microcalorimetry is a technique for measuring the heat absorbed or released when two compounds interact. Microcalorimeters can detect extremely small amounts of energy, as heat, often measured in microcalories, or μcal s.

11. Microcalorimetry has applications in research and development across several disciplines. For instance, in chemistry, researchers can use microcalorimetry to determine thermal properties of a substance. In biotechnology, researchers can use microcalorimetry to determine the binding strength between a drug and a protein to assess the viability of that drug in treating a medical condition. In materials engineering, researchers can

use microcalorimetry to determine the melting point of a new material composition, which is often critical information before deploying a new material in industry.

12. A microcalorimeter works by measuring the amount of energy a substance or mixture consumes or releases at a given temperature. One microcalorimeter configuration is the ITC.

13. In a typical ITC setup, there are two chambers: a sample cell and a reference cell. The sample cell contains a sample (for example, a protein) suspended in a buffer solution. The reference cell contains water or a buffer solution. A syringe and needle are used to titrate (i.e., deliver drop-by-drop) a ligand (a molecule that binds with the sample, for example, a drug) into the sample cell. During the experiment, the temperature in the two cells is held constant (hence the reference to “isothermal” in ITC).



14. A user begins an ITC experiment by controlling the syringe to introduce a measured amount of ligand (also called the titrant) into the sample cell. In some ITCs, a stirring assembly mixes the ligand and the sample. The resulting reaction either produces heat

(exothermic) or consumes heat (endothermic). The ITC measures the amount of energy it takes to keep the sample cell at the same temperature as the reference cell to which no ligand is added.

15. The compounds tested using microcalorimetry, known as “samples,” are often expensive and produced in small amounts. A single experiment may require multiple trials, with each trial requiring a fresh sample. Further, a failed or faulty experiment may require an entirely new sample. For these reasons, it is desirable for microcalorimeters to be designed to reduce the amount of sample needed for each experiment, a goal that was facilitated by Malvern’s patented technologies.

COMPANY BACKGROUND

16. MicroCal was, and as part of Malvern remains, a pioneer in microcalorimetry instrumentation. MicroCal founder Dr. John Brandts began his career in academia. In 1964, Dr. Brandts published a paper concerning modelling reversible protein denaturation, *i.e.*, the folding and unfolding of protein molecules that occurs with the introduction or removal of heat. Dr. Brandts theorized that proteins exist in only two states, native (folded) and denatured (unfolded), and that proteins do not exist in a partially folded state. To test this theory, Dr. Brandts needed to measure the heat exchange of reversible protein denaturation. This required a calorimeter of considerable measurement sensitivity, but such instruments were not commercially available in the 1960s. At the time, the most significant development of microcalorimeters was being conducted by Russian scientist Valerian Plotnikov in the Soviet Union, but these Russian instruments were not available to Dr. Brandts.

17. Dr. Brandts decided to develop his own calorimeter to meet his research needs. The result was a differential scanning calorimeter, or DSC, that was precise enough for

his purposes. Using his DSC, Dr. Brandts was able to show that his two-state model of reversible protein denaturation was correct.

18. In 1977, a large multinational corporation asked Dr. Brandts if he would sell them a version of his DSC. Dr. Brandts founded MicroCal to meet this need. Working from his basement, and relying on a local jeweler to craft prototype cells, Dr. Brandts assembled the first commercially-viable microcalorimeter instrument—the MC-1 differential scanning calorimeter, or MC-1 DSC. By the 1980s, Dr. Brandts had turned MicroCal into the world’s leading microcalorimeter instrumentation provider.

19. In 1989, Dr. Brandts and his colleagues at MicroCal introduced a new type of microcalorimeter, the Omega ITC, the world’s first commercially-available ITC.

20. MicroCal did not stop innovating. In the 1990s, MicroCal recruited Russian scientist Dr. Plotnikov, a world leader in the field of microcalorimetry, to lead MicroCal’s continued research and development efforts. Dr. Plotnikov oversaw the launch of new ITC lines, including the 2007 launch of the ITC200, a revolutionary instrument with a significantly smaller sample cell volume than earlier ITCs. Dr. Plotnikov was a co-inventor on several MicroCal patents, including two at issue here. Dr. Plotnikov’s inventions enable ITC experiments to be performed using significantly less sample material than earlier ITCs. MicroCal also developed the Auto ITC200, which permitted numerous experiments to be set up and conducted automatically, without the need for manual cell preparation and sample and titrant loading.

21. As part of Malvern, MicroCal’s current ITC offerings include the PEAQ ITC and PEAQ ITC Auto, successors to the ITC200 and Auto ITC200 respectively.

MALVERN'S PATENTED INVENTIONS

Plotnikov Patents

22. U.S. Patent No. 8,449,175 is entitled “Isothermal Titration Microcalorimeter Apparatus and Method of Use” (the “’175 Patent”). Malvern is the owner of all right, title, and interest in and to the ’175 Patent. The ’175 Patent issued on May 28, 2013, and claims priority to an earlier application filed November 1, 2007. Malvern submitted the ’175 Patent for supplemental examination in 2016, and a certificate of reexamination for the ’175 Patent issued on February 21, 2018. A true and accurate copy of the ’175 Patent is attached hereto as Exhibit A.

23. U.S. Patent No. 8,827,549 is also entitled “Isothermal Titration Microcalorimeter Apparatus and Method of Use” (the “’549 Patent”). The ’549 Patent is a continuation of the ’175 Patent and shares the same specification. Malvern is the owner of all right, title, and interest in and to the ’549 Patent. The ’549 Patent issued on September 9, 2014, and similarly claims priority to an earlier application filed November 1, 2007. Malvern submitted the ’549 Patent for supplemental examination in 2016, and a certificate of reexamination for the ’549 Patent issued on February 23, 2018. A true and accurate copy of the ’549 Patent is attached hereto as Exhibit B.

24. The inventions claimed in the ’175 Patent and ’549 Patent were invented by Valerian Plotnikov and Andrzej Rochalski. The ’175 Patent and ’549 Patent are hereinafter collectively referred to as the “Plotnikov Patents.”

25. The Plotnikov Patents disclose an improved ITC device that overcomes drawbacks found in prior art ITC devices. (*See, e.g.,* Ex. A, ’175 Patent, at 3:10-15.) For example, the Plotnikov Patents state that “the sensitivity of the ITC is improved, the amount of

biological substance necessary for testing is reduced, the reliability of the results generated by the ITC is improved, and use of the ITC is improved.” (*Id.* at 3:3-6.)

26. One advantage of the inventions disclosed in the Plotnikov Patents relates to reducing interference from the prior art ITC device’s stirring motor, which adversely affects measurement accuracy. Prior art ITCs included stirring motors and magnetic couplings located closely to the device’s sensitive thermal core (the sample and reference cells where the heat measurements are made), but this positioning created noise that interfered with the circuitry in the thermal core. (*See, e.g., Id.* at 2:50-55.) This noise limited the sensitivity of the measuring unit. (*Id.* at 2:55-67.)

27. The Plotnikov Patents provide solutions that reduce the interference from the stirring motor by placing the stirring motor away from the device’s sensitive thermal core. (*See, e.g., Id.* at 6:27-33.) “Accordingly, the sensitivity of the inventive ITC is raised by the lower power, the lower heat, the lower electricity, and the lower noise and vibration caused by the placement of the stirring motor as disclosed herein.” (*Id.* at 6:34-37.) With the increased sensitivity of the measuring unit, the size of the sample cell can be reduced “by about a factor of seven as compared to prior art ITCs” and experiments can be performed “with about 10 times less protein sample.” (*Id.* at 3:16-22.) Thus, practitioners can use less of the expensive sample when performing experiments, thereby saving significant cost. (*Id.* at 3:1-6). This facilitates the use of the technique in new areas, including wider application in biological systems.

28. Another drawback of prior art ITCs is that the practitioner needed to correctly align the titration needle with the sample cell without touching any part of the sample cell. (*Id.* at 2:8-10.) Misalignment could result in the needle breaking. Changing broken needles takes up valuable experiment time and purchasing new needles increases the cost of

consumables. The Plotnikov Patents address the alignment problem with the use of novel pipette guiding mechanisms and alignment components.

Broga Patents

29. U.S. Patent No. 9,404,876 is entitled “Automatic Isothermal Titration Microcalorimeter Apparatus and Method of Use” (the “’876 Patent”). Malvern is the owner of all right, title, and interest in and to the ’876 Patent. The ’876 Patent issued on August 2, 2016, and claims priority to December 2, 2008. A true and accurate copy of the ’876 Patent is attached hereto as Exhibit C.

30. U.S. Patent No. 10,036,715 is entitled “Automatic Isothermal Titration Microcalorimeter Apparatus and Method of Use” (the “’715 Patent”). The ’715 Patent is a continuation of the ’876 Patent and shares the same specification. Malvern is the owner of all right, title, and interest in and to the ’715 Patent. The ’715 Patent issued on July 31, 2018, and claims priority to an application filed December 2, 2008. A true and accurate copy of the ’715 Patent is attached hereto as Exhibit D.

31. U.S. Patent No. 10,254,239 is entitled “Automatic Isothermal Titration Microcalorimeter Apparatus and Method of Use” (the “’239 Patent”). The ’239 Patent is a continuation of the ’715 Patent and shares the same specification. Malvern is the owner of all right, title, and interest in and to the ’239 Patent. The ’239 Patent issued on April 9, 2019, and claims priority to December 2, 2008. A true and accurate copy of the ’239 Patent is attached hereto as Exhibit E.

32. The ’876, ’715, and ’239 Patents list Martin Broga, Phillip Price, and Stephen Smith as named inventors and are hereinafter collectively referred to as the “Broga Patents.”

33. The Broga Patents disclose an automated ITC device that improves upon prior-art devices. As discussed above, prior art ITC devices “require extensive preparation and skill by the practitioner.” (*See, e.g.*, Ex. C, ’876 Patent, at 1:56). Thus, the “quality of binding measurements performed with these prior art ITCs depends heavily [on] the operator’s skills and experience, and involves a considerable amount of preparation time.” (*Id.* at 2:13-16.) The Broga Patents address these problems by disclosing, among other things, automated titration, washing, and filling operations (*id.* at 5:14-16, 5:43-45), which reduces the practitioner involvement in the experiment to improve throughput and reliability of the experiments.

Patent Markings

34. Since at least 2015, Malvern has marked its MicroCal ITC instruments with a label notifying the public of its patents. Malvern generally marks its products in the following format: “Patent: malvern.com/patents.” This URL provides a link to a webpage that is directly accessible to the public and that contains a patent list associating each of Malvern’s products with the relevant Malvern patent numbers.

35. Since at least February 2015, Malvern’s online patent list included the patent numbers for the Plotnikov Patents. By August 13, 2019, Malvern’s online patent list was updated to show that the Plotnikov Patents had been re-examined. Since at least December 2016, Malvern’s online patent list included the ’876 Patent. Since at least August 2019, Malvern’s patent list included the ’715 and ’239 Patents.

THE ACCUSED PRODUCTS

Affinity ITC and Affinity ITC Auto Infringe Claims of the Plotnikov Patents

36. The TA Affinity ITC is a single-armed ITC, while the TA Affinity ITC Auto is a double-armed ITC.

37. The Affinity ITC and ITC Auto practice all limitations of exemplary independent claim 9 of the '175 Patent, and exemplary independent claim 1 of the '549 Patent.

38. Claim 9 of the '175 Patent recites:

A micro titration calorimetry system comprising:
an automatic pipette assembly comprising a titration needle
arranged to be inserted into a sample cell for supplying titrant, a
syringe for supplying titrant to the titration needle, a stirring paddle
for stirring fluid in the sample cell, and a stirring motor for rotating
the stirring paddle, and
a pipette guiding mechanism arranged to guide the pipette
assembly between and into at least two positions of operation,
wherein a first position of operation is a pipette washing position
wherein the titration needle is inserted in a washing apparatus, and
a second position of operation is a titration position wherein the
titration needle is inserted into the sample cell for calorimetric
measurements.



39. Claim 1 of the '549 Patent recites:

A micro titration calorimetry system comprising:
an automatic pipette assembly comprising a titration needle
arranged to be inserted into a sample cell for supplying titrant, a
syringe for supplying titrant to the titration needle, a stirring paddle
for stirring fluid in the sample cell, and a stirring motor for rotating
the stirring paddle, and

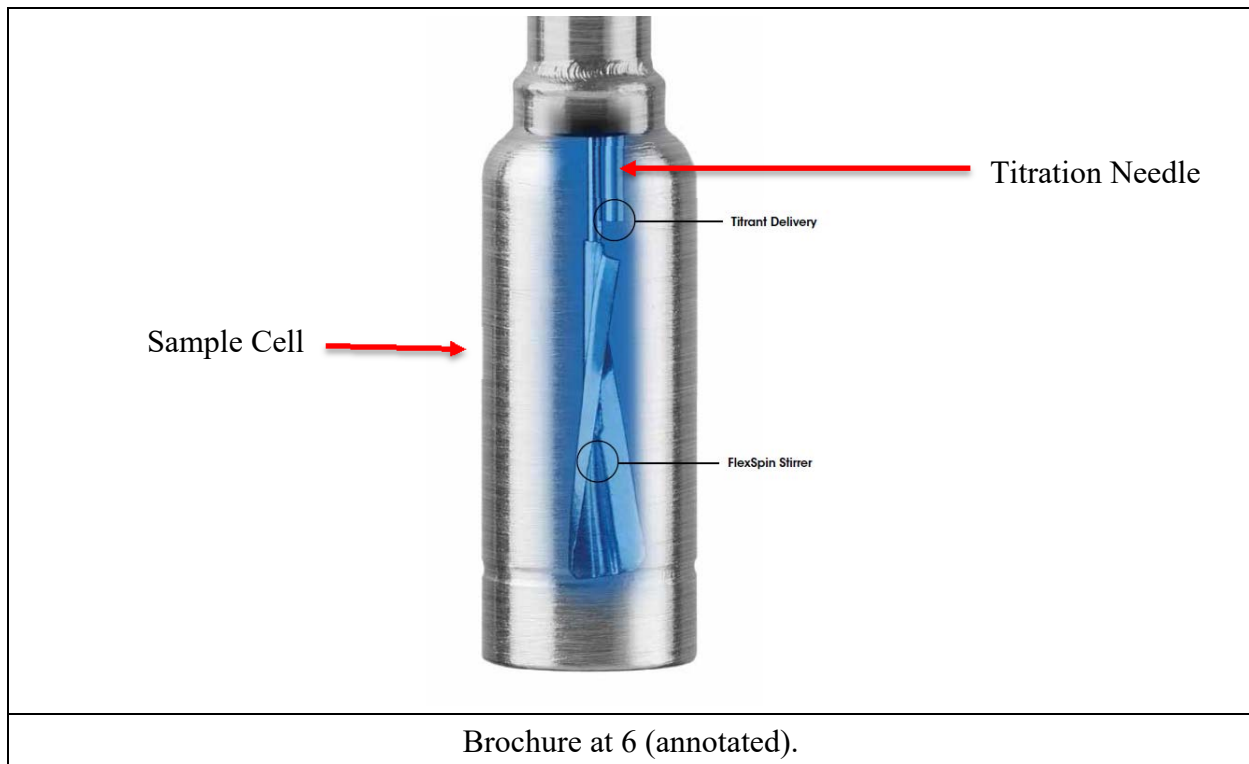
a pipette guiding mechanism arranged to restrict the movement of the pipette assembly along safe paths to ensure that the titration needle cannot be damaged during movement thereof between different positions of operation.

40. The Affinity ITC and Affinity ITC Auto are each “a micro titration calorimetry system” with an “automatic pipette assembly” containing a titration needle, a syringe, a stirring paddle, and a stirring motor, as recited in claim 9 of the ’175 Patent and claim 1 of the ’549 Patent. Defendants’ Brochure¹ is titled “Microcalorimetry: ITC & DSC” and indicates that the Affinity ITC and Affinity ITC Auto are “[i]sothermal [t]itration [c]alorimeter[s].” (Brochure at 3.) As described further below, the Brochure and Defendant’s promotional videos show that the Affinity ITC and Affinity ITC Auto each have a titration needle (*infra* ¶ 41), a syringe (*infra* ¶ 42), a stirring paddle (*infra* ¶ 43), and a stirring motor (*infra* ¶ 44), all contained within the automatic pipette assembly and which are used for conducting calorimetry experiments.

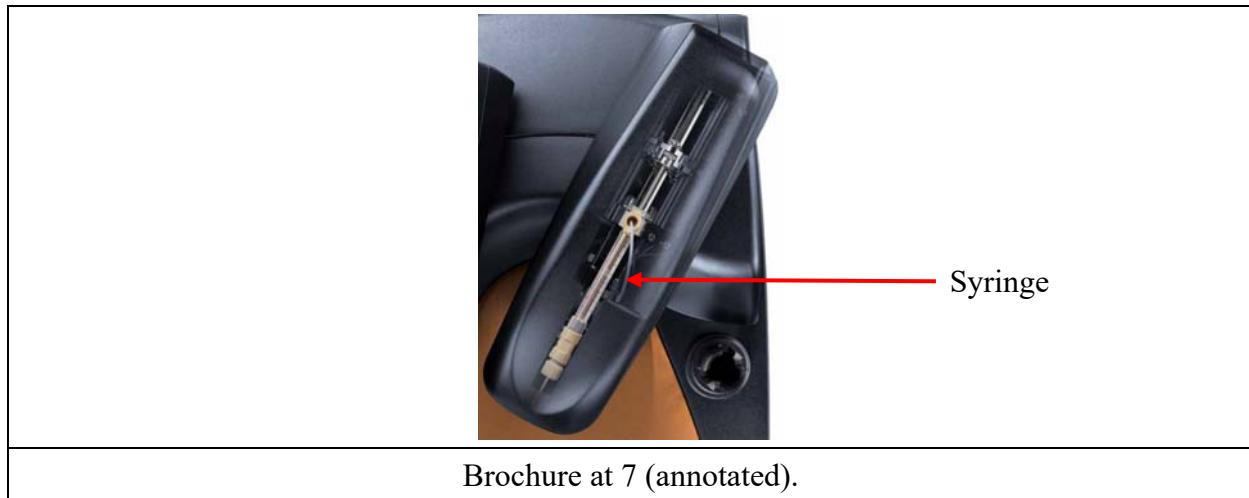
¹ *Microcalorimetry: ITC & DSC*, TA Instruments, at 3 (2019), available at: <https://www.tainstruments.com/wp-content/uploads/BROCH-MICRO-EN.pdf> (“Brochure”).

 <p>Automatic Pipette Assembly</p> <p>The image shows a single-armed Affinity ITC machine. A red arrow points from the text 'Automatic Pipette Assembly' to a vertical red line that indicates the position of the pipette assembly on the machine's arm.</p>	 <p>Automatic Pipette Assembly</p> <p>The image shows a double-armed Affinity ITC Auto machine. A red arrow points from the text 'Automatic Pipette Assembly' to a vertical red line that indicates the position of the pipette assembly on one of the machine's arms.</p>
<p>Single-armed Affinity ITC Brochure at 3 (annotated).</p>	<p>Double-armed Affinity ITC Auto Brochure at 3 (annotated).</p>

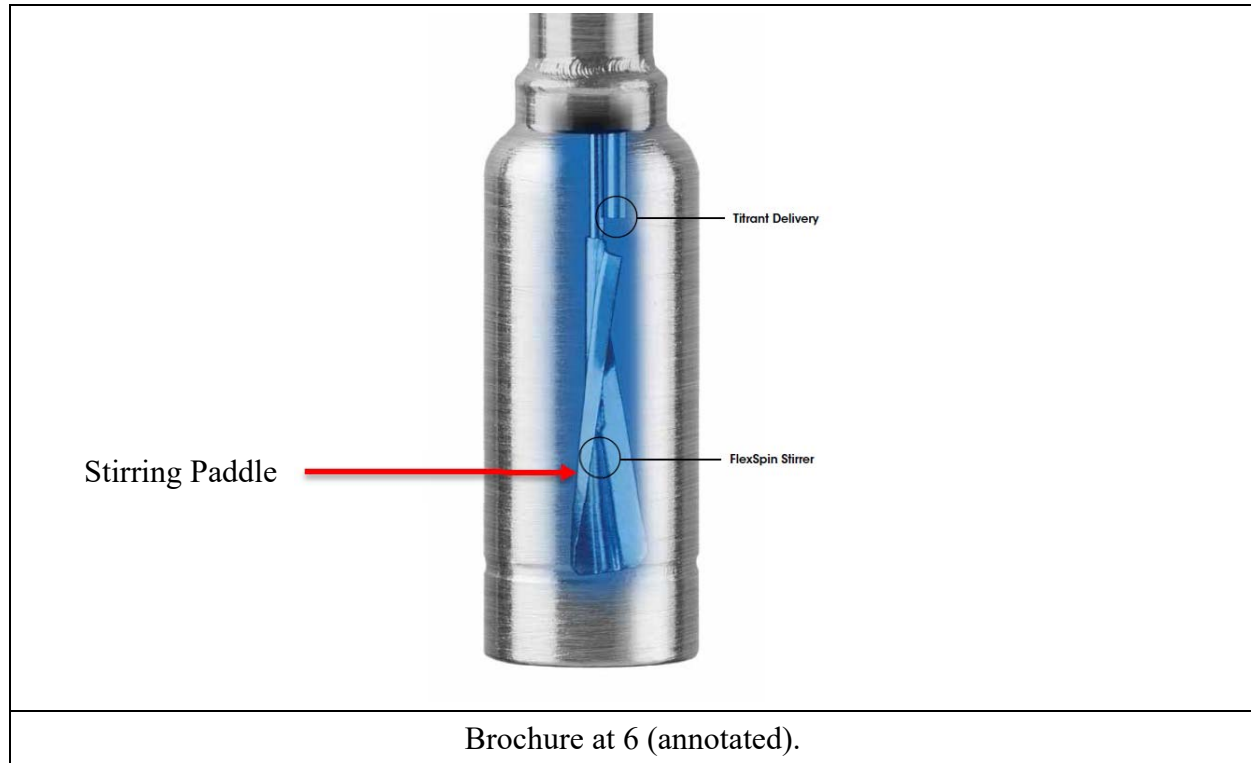
41. The Affinity ITC and ITC Auto each include “a titration needle arranged to be inserted into a sample cell for supplying titrant” as recited in claim 9 of the ’175 Patent and claim 1 of the ’549 Patent. The Brochure contains an image of the titration needle inserted into the sample cell and states that the titration needle is for “Titrant Delivery.” (Brochure at 6.)



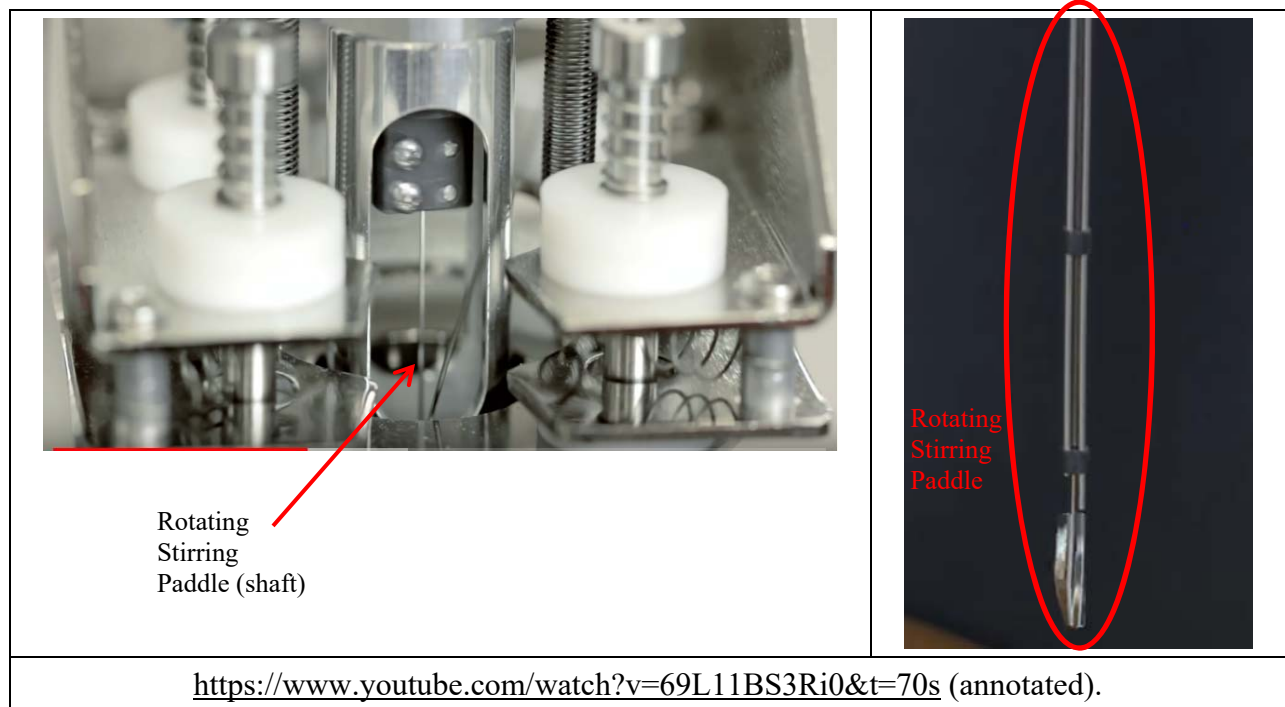
42. The Affinity ITC and ITC Auto each include “a syringe for supplying titrant to the titration needle” as recited in claim 9 of the ’175 Patent and claim 1 of the ’549 Patent. The Brochure contains an image of the syringe and states that there is a “[s]ingle syringe for all injection volumes and experiment designs,” and that the “[s]yringe needle [is] positioned to deliver titrant at the top of [the] stirring paddle.” (Brochure at 7.) Titrant from the syringe is supplied to the needle for injection into the sample cell.



43. The Affinity ITC and ITC Auto each include “a stirring paddle for stirring fluid in the sample cell” as recited in claim 9 of the ’175 Patent and claim 1 of the ’549 Patent. The Brochure includes an image of the stirring paddle inside the sample cell and highlights the “[r]evolutionary new paddle shape,” “[m]ore efficient mixing,” and “[s]lower stir speeds.” (Brochure at 6.)

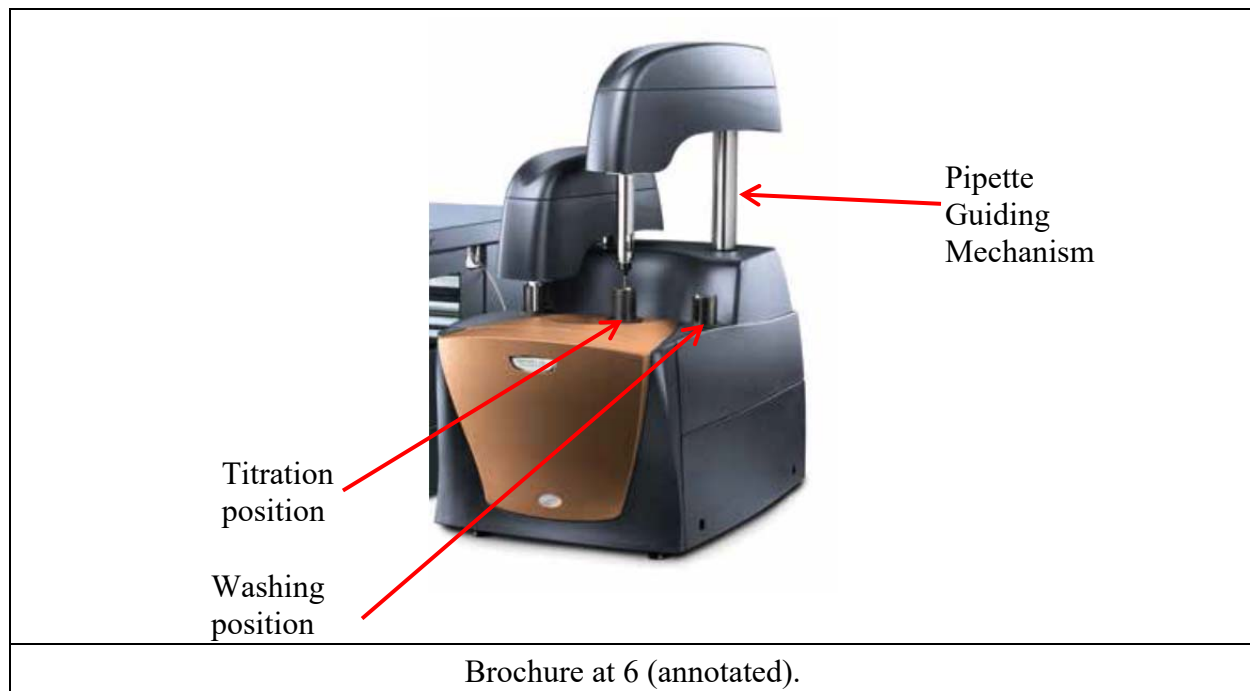


44. The Affinity ITC and ITC Auto each include “a stirring motor for rotating the stirring paddle” as recited in claim 9 of the ’175 Patent and claim 1 of the ’549 Patent. The below images are screen shots from one of Defendants’ promotional videos that show the rotating stirring paddle, driven by the stirring motor. The video states that the stirring paddle “is capable of slower stir speeds up to ten times slower than competitive instruments.” (See <https://www.youtube.com/watch?v=69L11BS3Ri0&t=70s>.)



45. The Affinity ITC and ITC Auto each include “a pipette guiding mechanism arranged to guide the pipette assembly between and into at least two positions of operation, wherein a first position of operation is a pipette washing position wherein the titration needle is inserted in a washing apparatus, and a second position of operation is a titration position wherein the titration needle is inserted into the sample cell for calorimetric measurements” as recited in claim 9 of the ’175 Patent. Defendants’ promotional videos show the pipette guiding mechanism rotating the pipette assembly between two operating positions, a pipette washing position wherein the titration needle is inserted in a washing apparatus, and a titration position wherein the titration needle is inserted into the sample cell in order to perform the calorimetric measurements.

(<https://www.youtube.com/watch?v=Ml6VFZPKVug&list=PL8C347B43BE9EF0C9&t=145s>.)



Brochure at 6 (annotated).

46. Defendants’ Brochure depicts and describes the washing apparatus into which the titration needle is inserted for cleaning (see below).



Dedicated Wash Station

Brochure at 11.

47. The pipette guiding mechanism of the Affinity ITC and Affinity ITC Auto is also “arranged to restrict the movement of the pipette assembly along safe paths to ensure that the titration needle cannot be damaged during movement thereof between different positions” as recited in claim 1 of the ’549 Patent. As shown in Defendants’ promotional videos, the pipette guiding mechanism moves the pipette assembly along safe paths, ensuring that the titration needle cannot be damaged during movement between different positions of operation. Defendants’ promotional videos promote these safe paths, stating that the Affinity ITC Auto “eliminates” the issues of “misalignment” and “broken and bent syringes” and “ensures accurate and reliable placement of automated hardware.”

(<https://www.youtube.com/watch?v=69L11BS3Ri0&t=127s>; *see also* Brochure at 10.)

Affinity ITC Auto Infringes Claims of the Broga Patents

48. The Affinity ITC Auto includes all limitations from exemplary independent claim 1 of the '876 Patent, exemplary independent claim 1 of the '715 Patent, and exemplary independent claim 1 of the '239 Patent.

49. Claim 1 of the '876 Patent recites:

An automated isothermal titration micro calorimetry (ITC) system,
comprising:

a controller configured to control automated operation of the ITC system, a micro calorimeter comprising a sample cell and a reference cell, the sample cell being accessible via a sample cell stem and the reference cell being accessible via a reference cell stem, a pipette assembly comprising a syringe, a titration needle configured to be inserted into the sample cell and supply titrant to the sample cell, and an activator configured to drive a plunger in a cavity of the syringe, a rotatable pipette translation unit comprising a rotatable pipette arm configured to support the pipette assembly and place the pipette assembly in a titration position and in a washing position, a rotatable cell preparation unit comprising a rotatable cell arm configured to wash the sample cell and replace sample liquid in the sample cell, the controller being configured to control operation of the ITC system to wash the syringe and titration needle of the pipette assembly, fill the syringe with new

titrant, wash the sample cell, and fill the sample cell with new sample liquid.

50. Claim 1 of the '715 Patent recites:

An isothermal titration micro calorimetry (ITC) system, comprising;

a microcalorimeter,

a pipette assembly comprising a syringe with a fill port configured to provide fluidic contact with a cavity of the syringe and an activator configured to drive a plunger in the cavity of the syringe, a rotatable pipette translation unit configured to place the pipette assembly in a titration position and in a washing position, a rotatable cell preparation unit configured to wash a sample cell of the microcalorimeter and replace sample liquid in the sample cell when the pipette assembly is placed in another position than the position for titration, and

a fill port connection unit comprising a connection member configured to connect to the fill port thereby enabling fluid to transfer into the cavity of the syringe.

51. Claim 1 of the '239 Patent recites:

An automated isothermal titration micro calorimetry (ITC) system, comprising:

a controller configured to control automated operation of the ITC system;

a microcalorimeter comprising a sample cell and a reference cell, the sample cell being accessible via a sample cell stem and the reference cell being accessible via a reference cell stem;

a pipette assembly comprising a titration needle configured to be inserted into the sample cell and supply titrant to the sample cell;

a rotatable pipette translation unit comprising a rotatable pipette arm configured to support the pipette assembly and place the pipette assembly in a titration position and in a washing position, wherein the rotatable pipette arm is configured to be moved vertically along an axis and the titration needle is vertically moveable in the direction of the axis for insertion into the sample cell; and

a rotatable cell preparation unit comprising a rotatable cell arm configured to wash the sample cell and replace sample liquid in the sample cell,

wherein the controller is configured to control operation of the ITC system to wash the titration needle of the pipette assembly, wash the sample cell, and fill the sample cell with sample liquid.

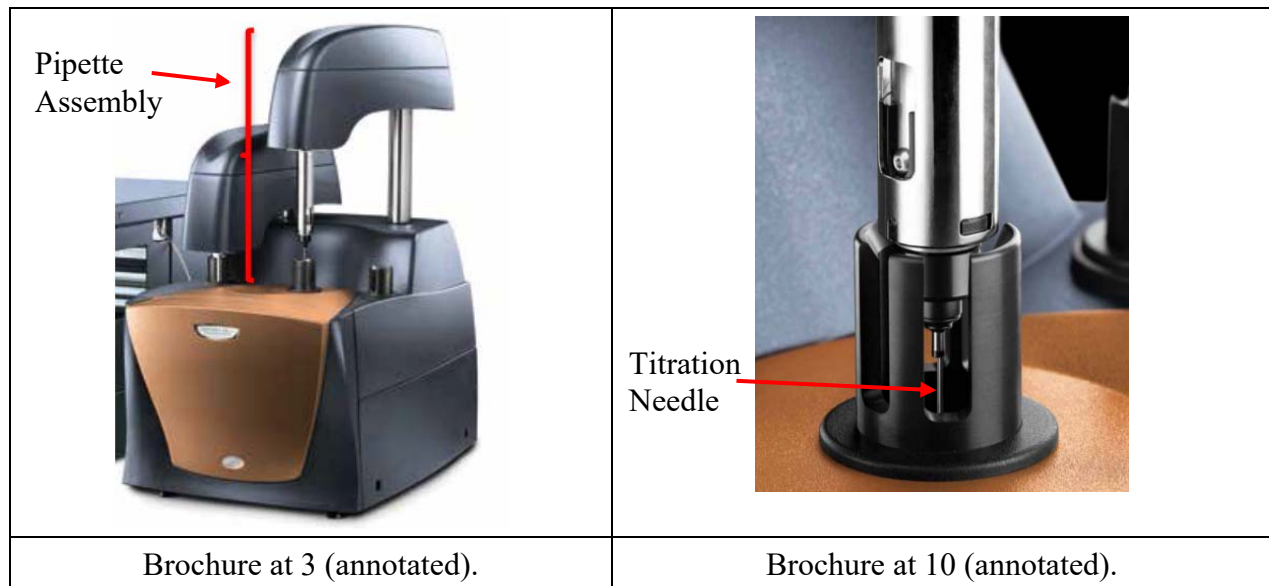
52. The Affinity ITC Auto's "Intelligent Hardware Positioning" (Brochure at 3, 10) and "control software" (*id.* at 13) running on a controller allow for automated operation of the Affinity ITC Auto (*see id.* at 8 (describing Affinity ITC Auto as "the most powerful platform for automated . . . ITC experiments")). Accordingly, the Affinity ITC Auto practices "a



controller configured to control automated operation of the ITC system” as recited in claim 1 of the ’876 Patent and claim 1 of the ’239 Patent.

53. The Affinity ITC Auto includes a “microcalorimeter” recited in claim 1 of the ’715 Patent, with “a sample cell and a reference cell, the sample cell being accessible via a sample cell stem and the reference cell being accessible via a reference cell stem” as recited in the ’876 and ’239 Patents. The Brochure states that the Affinity ITC Auto includes “two fixed-in-place calorimetric cells: a sample cell where injections take place and a matching reference cell.” (Brochure at 4.) Defendants’ promotional video shows the sample and reference cells, as well as the cell stems through which the cells are accessed (see below).




54. The Affinity ITC Auto includes a “pipette assembly” (shown in the image below) as recited in claim 1 of the ’876 Patent, claim 1 of the ’715 Patent, and claim 1 of the ’239 Patent. The pipette assembly includes “a titration needle configured to be inserted into the sample cell and supply titrant to the sample cell” as recited in claim 1 of the ’876 and claim 1 of the ’239 Patents, and a “syringe” and an “activator configured to drive a plunger in a cavity of the syringe” as recited in claim 1 of the ’876 and claim 1 of the ’715 Patents. The plunger driving into the cavity of the syringe can be seen in Defendants’ promotional videos. (*See* <https://www.youtube.com/watch?v=69L11BS3Ri0&t=90s.>) The syringe also includes “a fill port configured to provide fluidic contact with a cavity of the syringe,” as recited in claim 1 of the ’715 Patent. The Brochure states that the Affinity ITC Auto features “[e]asy titrant loading without injection syringe removal.” (Brochure at 7.) In other words, the cavity of the syringe can be filled with titration fluid without removing the syringe from the pipette assembly.

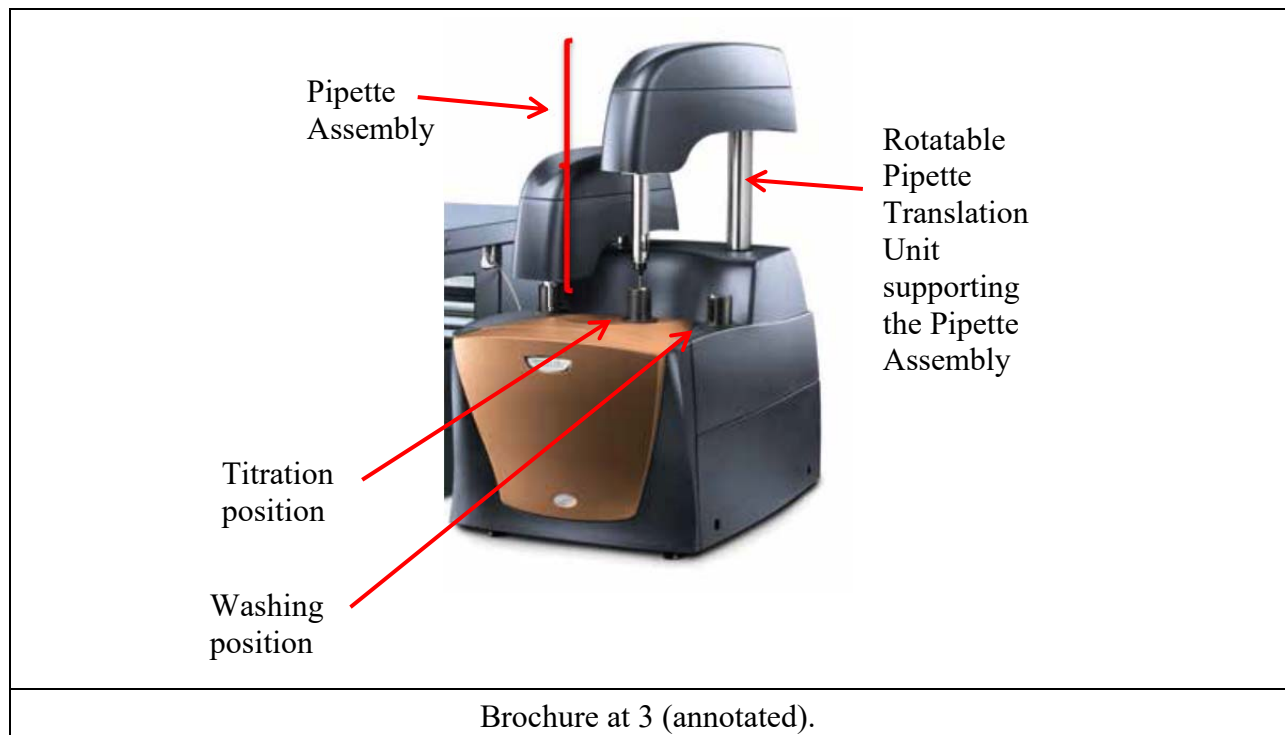




 <p>Fill Port</p> <p>Syringe</p>	 <p>Syringe</p> <p>Plunger</p> <p>AccuShot</p>
<p>Brochure at 7 (annotated).</p>	<p>https://www.youtube.com/watch?v=69L11BS3Ri0&t=90s (annotated).</p>

55. The Affinity ITC Auto includes a “rotatable pipette translation unit” to, among other things, “place the pipette assembly in a titration position and in a washing position” as recited in claim 1 of the ’876, claim 1 of the ’239, and claim 1 of the ’715 Patents. Defendants’ promotional videos show the Affinity ITC Auto’s pipette translation unit rotating the pipette assembly between a washing position and a titration position. (See <https://www.youtube.com/watch?v=Ml6VFZPKVug&list=PL8C347B43BE9EF0C9&t=145s.>)

 <p>Rotatable Pipette Translation Unit</p> <p>Titration position</p> <p>Washing position</p>	<p>Brochure at 3 (annotated).</p>
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56. The rotatable pipette translation unit “support[s] the pipette assembly” as recited in claim 1 of the ’876 and claim 1 of the ’239 Patents and is “configured to be moved vertically along an axis and the titration needle is vertically moveable in the direction of the axis for insertion into the sample cell” as recited in claim 1 of the ’239 Patent. The Brochure depicts the Affinity ITC Auto’s pipette translation unit supporting the pipette assembly (*see* Brochure at 3). Defendant’s promotional videos show the pipette translation unit rotating the pipette assembly between a washing position and a titration position (*see* <https://www.youtube.com/watch?v=Ml6VFZPKVug&list=PL8C347B43BE9EF0C9&t=145s.>), and show the pipette translation unit and pipette assembly moving vertically to insert the titration needle into the sample cell (*see* <https://www.youtube.com/watch?v=Ml6VFZPKVug&list=PL8C347B43BE9EF0C9&t=143s.>)



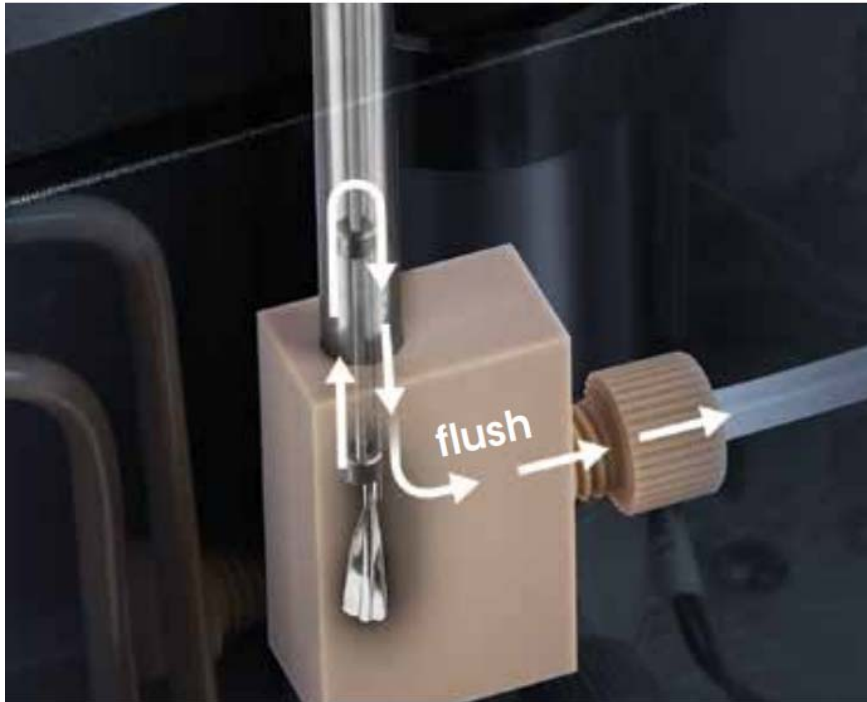
 <p data-bbox="219 800 711 835">Titration position Washing position</p>	
<p data-bbox="209 869 771 976"> https://www.youtube.com/watch?v=Ml6VFZPKVug&list=PL8C347B43BE9EF0C9&t=85s (rotating motion from washing to titration position) (annotated). </p>	<p data-bbox="839 869 1414 1056"> https://www.youtube.com/watch?v=Ml6VFZPKVug&list=PL8C347B43BE9EF0C9&t=143s (vertical motion for insertion into the sample cell) (annotated). </p>

57. The Affinity ITC Auto includes “a rotatable cell preparation unit” that is “configured to wash the sample cell” and to “replace sample liquid in the sample cell” as recited in claim 1 of the ’876 Patent, claim 1 of the ’715 Patent, and claim 1 of the ’239 Patent. This occurs “when the pipette assembly is placed in another position than the position for titration” as recited in the ’715 Patent. The rotatable cell preparation unit also includes “a rotatable cell arm” as recited in claim 1 of the ’876 and claim 1 of the ’239 Patents. Defendants’ promotional videos show the pipette assembly moving from the titration position to the washing position and the cell preparation unit rotating into the titration position to prepare the sample cell for the next experiment. (See <https://www.youtube.com/watch?v=69L11BS3Ri0&t=170s>.) Additionally, the Brochure states that “[t]he automated cleaning system engineered into the Affinity ITC Auto instrument ensures that the entire system is cleaned between sample titrations” and that there are “[d]edicated wash/rinse stations for . . . cell cleaning/filling.” (Brochure at 11.)



58. The controller of the Affinity ITC Auto is further “configured to control operation of the ITC system” to wash the syringe, titration needle, and sample cell, to fill the syringe with new titrant, and to fill the sample cell with new sample liquid as recited in claim 1 of the ’876 Patent and claim 1 of the ’239 Patent. The Brochure states that the Affinity ITC Auto includes an automated cleaning system that “ensures that the *entire system* is cleaned between sample titrations.” (Brochure at 11 (emphasis added); *see also* <https://www.youtube.com/watch?v=69L11BS3Ri0&t=140s>.) The Affinity ITC Auto’s automated cleaning system includes “[d]edicated wash/rinse stations for stirring/injection syringes and cell cleaning/filling.” (Brochure at 11.) The Affinity ITC Auto also provides for “easy titrant loading without injection syringe removal” and “[f]ully automated internal and external cleaning of injection cannula.” (Brochure at 7.)





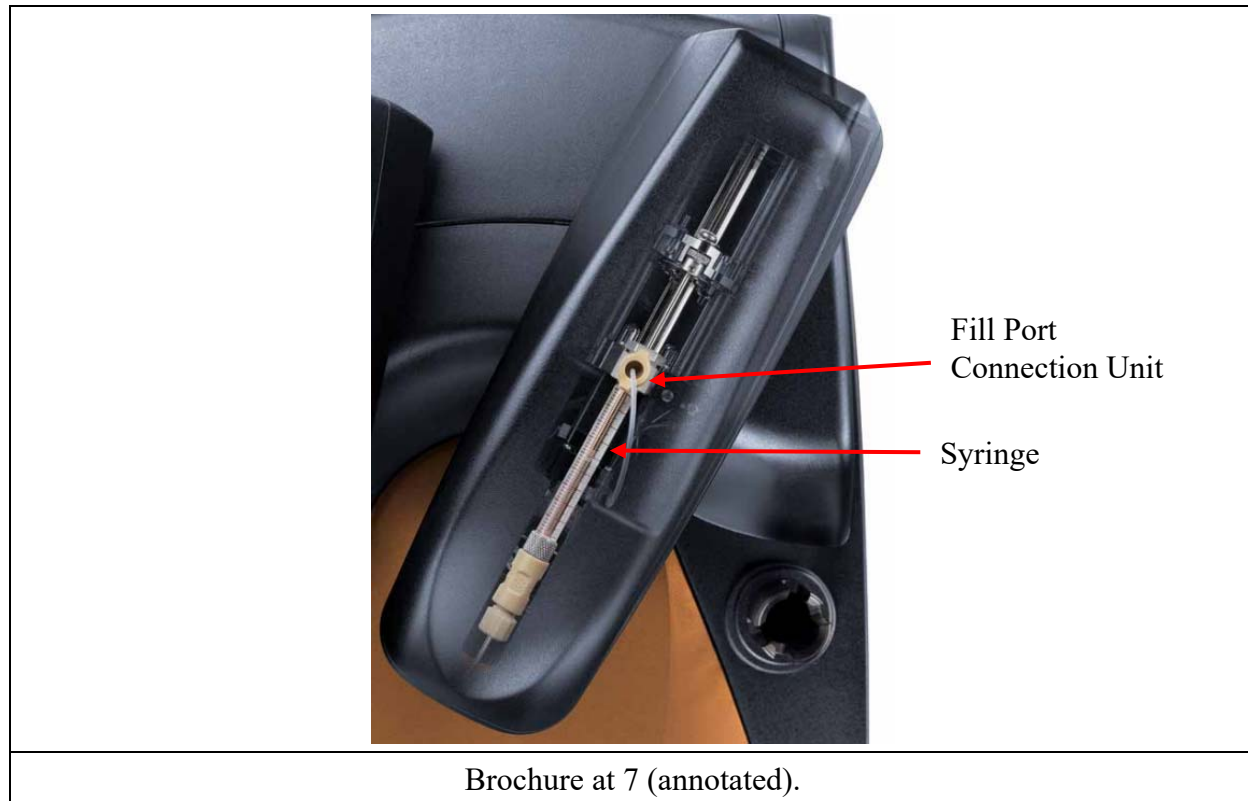
Dedicated Wash Station

Brochure at 11 (annotated).

	Affinity ITC Auto	Affinity ITC
Injection/Stirring cleaning	Fully automated	Fully automated
Cell cleaning	Fully automated	Cleaning tool
Cell filling cleaning	Fully automated	Manual

Brochure at 11.

59. The Affinity ITC Auto includes “a fill port connection unit comprising a connection member configured to connect to the fill port thereby enabling fluid to transfer into the cavity of the syringe” (shown in the image below) as recited in claim 1 of the ’715 Patent.



Brochure at 7 (annotated).

DEFENDANTS’ KNOWLEDGE OF THE ASSERTED PATENTS

60. Defendants and Malvern are the only two major competitors in the highly specialized and technical market for ITCs. Defendants directly compete with Malvern and market and sell the Affinity ITC and Affinity ITC Auto to the same or similar customers as Malvern.

61. On information and belief, Defendants have had possession of or have seen Malvern’s MicroCal ITC instruments with patent markings identifying the URL for Malvern’s patent list. Thus, Defendants knew or should have known of Malvern’s asserted patents on at least the basis of Malvern’s patent list posted on the Internet.

62. Additionally, on September 2, 2015, Malvern sent a letter to TA Instruments asserting infringement of the '175 and '549 Patents by the Affinity ITC and Affinity ITC Auto instruments. This letter also enclosed preliminary exemplary claim charts demonstrating how the Affinity ITC Auto infringed.

63. On information and belief, at least after receiving Malvern's September 2, 2015 letter, Defendants have monitored and continue to monitor Malvern's patent portfolio relating to ITCs.

64. On information and belief, Defendants knew or should have known that the Affinity ITC and Affinity ITC Auto infringed the asserted patents, at least after receiving Malvern's September 2, 2015 letter.

COUNT I
Infringement of U.S. Patent No. 8,449,175

65. Malvern repeats and re-alleges each of the allegations in paragraphs 1-64 of this Complaint.

66. Defendants have been and are now directly infringing, either literally or under the doctrine of equivalents, at least claims 9, 12, 14-18, 20, 24, 27, and 28 of the '175 Patent by manufacturing, using, selling, distributing, licensing, and/or offering for sale the Affinity ITC and Affinity ITC Auto without the authority of Malvern.

67. Defendants, without the authority of Malvern, have been and are now knowingly inducing their customers to directly infringe one or more of claims 9, 12, 14-18, 20, 24, 27, and 28 of the '175 Patent. Such inducements include inducing customers to use the Affinity ITC and/or Affinity ITC Auto knowing that such use infringes one or more claims of the '175 Patent, with specific intent to encourage the infringement. Defendants induce their customers to infringe the claims of the '175 Patent at least by instructing their customers to

operate the Affinity ITC and Affinity ITC Auto in accordance with the instructions Defendants provide through, without limitation, product brochures, manuals, specifications, and customer support services, offered on Defendants' website and through in-person and telephonic communications.

68. Defendants, without the authority of Malvern, have been and are now knowingly contributing to their customers' direct infringement of one or more of claims 9, 12, 14-18, 20, 24, 27, and 28 of the '175 Patent by selling or offering to sell their customers the Affinity ITC and/or Affinity ITC Auto and providing instructions for using those products, knowing that such use infringes the '175 Patent. The Affinity ITC and Affinity ITC auto are specifically designed in a manner that infringes the '175 Patent, and have no substantial non-infringing uses.

69. As recited above, Defendants' infringement has been willful, wanton, and deliberate, and in knowing and flagrant disregard of Malvern's patent rights.

70. Malvern has been and will be damaged and harmed by Defendants' infringement.

71. Malvern will be irreparably harmed unless Defendants' infringing activities are enjoined.

72. Malvern has no adequate remedy at law.

COUNT II
Infringement of U.S. Patent No. 8,827,549

73. Malvern repeats and re-alleges each of the allegations in paragraphs 1-64 of this Complaint.

74. Defendants have been and are now directly infringing, either literally or under the doctrine of equivalents, at least claims 1, 2, 5, 7-11, 13-14, 17, and 18 of the '549

Patent by manufacturing, using, selling, distributing, licensing, and/or offering for sale of the Affinity ITC and Affinity ITC Auto without the authority of Malvern.

75. Defendants, without the authority of Malvern, have been and are now knowingly inducing their customers to directly infringe one or more of claims 1, 2, 5, 7-11, 13-14, 17, and 18 of the '549 Patent. Such inducements include inducing customers to use the Affinity ITC and/or Affinity ITC Auto knowing that such use infringes one or more claims of the '549 Patent, with specific intent to encourage the infringement. Defendants induce their customers to infringe the claims of the '549 Patent at least by instructing their customers to operate the Affinity ITC and Affinity ITC Auto in accordance with the instructions Defendants provide through, without limitation, product brochures, manuals, specifications, and customer support services, offered on Defendants' website and through in-person and telephonic communications.

76. Defendants, without the authority of Malvern, have been and are now knowingly contributing to their customers' direct infringement of one or more of claims 1, 2, 5, 7-11, 13-14, 17, and 18 of the '549 Patent by selling or offering to sell their customers the Affinity ITC and/or Affinity ITC Auto and providing instructions for using those products, knowing that such use infringes the '549 Patent. The Affinity ITC and Affinity ITC auto are specifically designed in a manner that infringes the '549 Patent, and have no substantial non-infringing uses.

77. As recited above, Defendants' infringement has been willful, wanton, and deliberate, and in knowing and flagrant disregard of Malvern's patent rights.

78. Malvern has been and will be damaged and harmed by Defendants' infringement.

79. Malvern will be irreparably harmed unless Defendants' infringing activities are enjoined.

80. Malvern has no adequate remedy at law.

COUNT III
Infringement of U.S. Patent No. 9,404,876

81. Malvern repeats and re-alleges each of the allegations in paragraphs 1-64 of this Complaint.

82. Defendants have been and are now directly infringing, either literally or under the doctrine of equivalents, at least claims 1, 3-8, and 10-14 of the '876 Patent by manufacturing, using, selling, distributing, licensing, and/or offering for sale of the Affinity ITC Auto without the authority of Malvern.

83. Defendants, without the authority of Malvern, have been and are now knowingly inducing their customers to directly infringe one or more of claims 1, 3-8, and 10-14 of the '876 Patent. Such inducements include inducing customers to use the Affinity ITC Auto knowing that such use infringes one or more claims of the '876 Patent, with specific intent to encourage the infringement. Defendants induce their customers to infringe the claims of the '876 Patent at least by instructing their customers to operate the Affinity ITC Auto in accordance with the instructions Defendants provide through, without limitation, product brochures, manuals, specifications, and customer support services, offered on Defendants' website and through in-person and telephonic communications.

84. Defendants, without the authority of Malvern, have been and are now knowingly contributing to their customers' direct infringement of one or more of claims 1, 3-8, and 10-14 of the '876 Patent by selling or offering to sell their customers the Affinity ITC Auto and providing instructions for using that product, knowing that such use infringes the '876

Patent. The Affinity ITC Auto is specifically designed in a manner that infringes the '876 Patent, and has no substantial non-infringing uses.

85. As recited above, Defendants' infringement has been willful, wanton, and deliberate, and in knowing and flagrant disregard of Malvern's patent rights.

86. Malvern has been and will be damaged and harmed by Defendants' infringement.

87. Malvern will be irreparably harmed unless Defendants' infringing activities are enjoined.

88. Malvern has no adequate remedy at law.

COUNT IV
Infringement of U.S. Patent No. 10,036,715

89. Malvern repeats and re-alleges each of the allegations in paragraphs 1-64 of this Complaint.

90. Defendants have been and are now directly infringing, either literally or under the doctrine of equivalents, at least claims 1-11 of the '715 Patent by manufacturing, using, selling, distributing, licensing, and/or offering for sale of the Affinity ITC Auto without the authority of Malvern.

91. Defendants, without the authority of Malvern, have been and are now knowingly inducing their customers to directly infringe one or more of claims 1-11 of the '715 Patent. Such inducements include inducing customers to use the Affinity ITC Auto knowing that such use infringes one or more claims of the '715 Patent, with specific intent to encourage the infringement. Defendants induce their customers to infringe the claims of the '715 Patent at least by instructing their customers to operate the Affinity ITC Auto in accordance with the instructions Defendants provide through, without limitation, product brochures, manuals,

specifications, and customer support services, offered on Defendants' website and through in-person and telephonic communications.

92. Defendants, without the authority of Malvern, have been and are now knowingly contributing to their customers' direct infringement of one or more of claims 1-11 of the '715 Patent by selling or offering to sell their customers the Affinity ITC Auto and providing instructions for using that product, knowing that such use infringes the '715 Patent. The Affinity ITC Auto is specifically designed to operate in a manner that infringes the '715 Patent, and has no substantial non-infringing uses.

93. As recited above, Defendants' infringement has been willful, wanton, and deliberate, and in knowing and flagrant disregard of Malvern's patent rights.

94. Malvern has been and will be damaged and harmed by Defendants' infringement.

95. Malvern will be irreparably harmed unless Defendants' infringing activities are enjoined.

96. Malvern has no adequate remedy at law.

COUNT V
Infringement of U.S. Patent No. 10,254,239

97. Malvern repeats and re-alleges each of the allegations in paragraphs 1-64 of this Complaint.

98. Defendants have been and are now directly infringing, either literally or under the doctrine of equivalents, at least claims 1-6, 8, 9, 11-24, and 26-30 of the '239 Patent by manufacturing, using, selling, distributing, licensing, and/or offering for sale of the Affinity ITC Auto without the authority of Malvern.

99. Defendants, without the authority of Malvern, have been and are now knowingly inducing their customers to directly infringe one or more of claims 1-6, 8, 9, 11-24, and 26-30 of the '239 Patent. Such inducements include inducing customers to use the Affinity ITC Auto knowing that such use infringes one or more claims of the '239 Patent, with specific intent to encourage the infringement. Defendants induce their customers to infringe the claims of the '239 Patent at least by instructing their customers to operate the Affinity ITC Auto in accordance with the instructions Defendants provide through, without limitation, product brochures, manuals, specifications, and customer support services, offered on Defendants' website and through in-person and telephonic communications.

100. Defendants, without the authority of Malvern, have been and are now knowingly contributing to their customers' direct infringement of one or more of claims 1-6, 8, 9, 11-24, and 26-30 of the '239 Patent by selling or offering to sell their customers the Affinity ITC Auto and providing instructions for using that product, knowing that such use infringes the '239 Patent. The Affinity ITC Auto is specifically designed in a manner that infringes the '239 Patent, and has no substantial non-infringing uses.

101. As recited above, Defendants' infringement has been willful, wanton, and deliberate, and in knowing and flagrant disregard of Malvern's patent rights.

102. Malvern has been and will be damaged and harmed by Defendants' infringement.

103. Malvern will be irreparably harmed unless Defendants' infringing activities are enjoined.

104. Malvern has no adequate remedy at law.

PRAYER FOR RELIEF

WHEREFORE, Malvern respectfully prays that judgment be entered for Malvern and against Defendants as follows:

- A. Finding that Defendants have willfully infringed the Asserted Patents.
- B. Preliminarily and permanently enjoining Defendants, their officers, agents, servants, employees, attorneys, and those persons acting for, with, by, under, in privity with, in active consort with, and in participation with them (including affiliates and those in joint ventures with them), from manufacturing, using, selling, licensing, importing, exporting and/or offering for sale any product which infringes the Asserted Patents, and from inducing or contributing to infringement of the Asserted Patents.
- C. Awarding Malvern the damages it sustained as a result of Defendants' patent infringement, including, but not limited to, a reasonable royalty and/or lost profits.
- D. Awarding Malvern enhanced damages under 35 U.S.C. § 284 as a result of Defendants' willful patent infringement.
- E. Finding this to be an exceptional case under 35 U.S.C. § 285 and awarding Malvern its attorney fees.
- F. Awarding Malvern its costs incurred in this action.
- G. Granting Malvern such other and further relief as the Court may deem just, proper, and appropriate.

JURY TRIAL DEMAND

Pursuant to Fed. R. Civ. P. 38(b), Plaintiff demands a trial by jury on all issues so triable.

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January 23, 2020

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CERTIFICATE OF SERVICE

I hereby certify that on January 23, 2020, I caused the foregoing to be electronically filed with the Clerk of the Court using CM/ECF, which will send notification of such filing to all registered participants.

I further certify that I caused copies of the foregoing document to be served on January 23, 2020, upon the following in the manner indicated:

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